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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/522,106	07/26/2007	Karl-Heinz Kogel	12810-00067-US	9243

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EXAMINER	
IBRAHIM, MEDINA AHMED	

ART UNIT	PAPER NUMBER
1638	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/522,106	KOGEL ET AL.	
	Examiner	Art Unit	
	Medina A. Ibrahim	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 June 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 January 2009* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-23 and SEQ ID NO: 2 in the reply filed on 06/29/09 is acknowledged. The traversal is on the ground(s) that Applicant submits that all the claims in the application relate to a single inventive concept, namely, generating or increasing resistance to pathogens in plants by reducing the quantity, activity or function of an NADPH activity. Applicant also argues that the polypeptide sequences of SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, and 22 are all NADPH oxidizes, therefore, are related to a single inventive concept. Applicant makes an argument against search burden and asserts that all claims and sequences can be examined in a single application without undue search upon the Office. Applicant further argues that Chapter § 10 (10.06) of the International Search and Preliminary Examination Guidelines states that if the independent claims avoid the prior art and satisfy the requirement of unity, no lack of unity problem arises from the dependent claims even if it contain a further invention. Applicant, therefore, requests that all claims and all the sequences be examined together in this application.

These are not found persuasive for the following reasons: firstly, while the claimed invention in general relates to a method of increasing resistance to pathogens in plants by reducing the quantity/activity/function of an NADPH activity, each invention as listed in the restriction action requires specific product and steps that are not required by any of the other inventions. Neither Applicant's arguments nor the prior art establishes a relationship between the different method steps and different products of

reducing the quantity/activity/function of an NADPH activity as recited in the claims. For example, there is no known relationship between the use of dsRNA and the use of a ribozyme, DNA- or protein-binding factors against NADPH oxidase or viral nucleic acid sequences. Secondly, Applicant is reminded that the restriction requirement between inventions I-V is subject to the non-allowance of the generic claim 1. Thirdly, the specification does not provide a significant structural element common to all the sequences recited in the claims. Absent such a significant common structural elements, the sequences of the claims lack unity. Fourthly, since this application is filed under 371, search burden is not a consideration under lack of unity requirements. Finally, Applicant makes an argument that International Searching and Examination Authority found no lack of unity of the invention and therefore, PTO should not have raised objection as to a lack of unity. However, the U.S. Patent Office is not bound to maintain unity of invention findings in the U.S. national stage that were found in International Phase of international applications that designate, but do not originate in, the United States. See 35 U.S.C. 372(b)(2). PCT/EP03/07589 did not originate in the United States.

Therefore, the requirement is still deemed proper and is therefore made FINAL.

Claims 1-23 are pending. Claims 1-23, drawn to sense/antisense dsRNA of a DNA encoding SEQ ID NO: 2 or the nucleic acid of SEQ ID NO: 1 are examined.

Sequence Listings

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1)

and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825. For example, page 24 of the specification contain sequences which must be referred to by their sequence identifiers as required by 37 CFR 1.821. Applicant is required to identify the sequences or provide Sequence listings that contain the sequences. Applicant is also required to amend the specification, page 24, to include the sequence identifier. New matter should be avoided.

Specification

The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) TITLE OF THE INVENTION.
(b) CROSS-REFERENCE TO RELATED APPLICATIONS.
(c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
(d) THE NAMES OF THE PARTIES TO A JOINT RESEARCH AGREEMENT.
(e) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC.
(f) BACKGROUND OF THE INVENTION.
    (1) Field of the Invention.
    (2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
(g) BRIEF SUMMARY OF THE INVENTION.
(h) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
(i) DETAILED DESCRIPTION OF THE INVENTION.
(j) CLAIM OR CLAIMS (commencing on a separate sheet).
(k) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
(l) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if

the required "Sequence Listing" is not submitted as an electronic document on compact disc).

The specification is specifically objected to for lacking parts (f) to (i).

The specification on pages 66 and 68, lines 16 and 36, respectively, refer to figure 4; however, no fig 4 is submitted with the application. Only Fig. 1 drawing is provided and the description of Figures describes Fig. 1.

Claim Objections

Claims 1-23 are objected to for reciting non-elected invention. Claims 2-3 and 12-13 recite non-elected sequences and claims 4-5 and 21 recite a non-elected invention. Appropriate correction is required.

At claim 1, part (b), "-" should be replaced with ---,--- in each occurrences.

At claim 2, it is suggested that "is encoded by" be replaced with ---comprises--- because a polypeptide cannot encode another polypeptide (NADPH oxidase).

Claims 13 and 17-20 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from another multiple claim. See MPEP § 608.01(n).

Copending Applications

Applicants must bring to the attention of the Examiner, or other Office official involved with the examination of a particular application, information within their knowledge as to other copending United States applications, which are "material to patentability" of the application in question. MPEP 2001.06(b). See *Dayco Products Inc. v. Total Containment Inc.*, 66 USPQ2d 1801 (CA FC 2003).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for dsRNA comprising an isolated nucleic acid sequence encoding SEQ ID NO: 2 or the nucleic acid sequence of SEQ ID NO: 1; an expression cassette comprising said dsRNA sequences, and a method of generating or increasing at least one pathogen resistance in a plant/cell/part/or progeny thereof using dsRNA nucleic acid sequences, and transgenic plants comprising said nucleic acid sequences, does not reasonably provide enablement for a method that employs sense, antisense or dsRNA of nucleic acids encoding a functional equivalent of SEQ ID NO: 2 or sequences thereof having 50% homology, or sequences which are identical or complementary to a part of SEQ ID NO: 1 or to a part of a nucleic acid encoding SEQ ID NO:2 or a functional equivalent thereof and having antisense, sense and/or dsRNA inhibition activity function, and a transgenic animal comprising nucleic acid encoding a NADPH oxidase. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with these claims.

The claims are drawn to, *inter alia*, a method for generating or increasing a resistance to at least one plant pathogen which comprises reducing an amount, function or activity of a NADPH oxidase in a plant or tissue, organ, part or cell thereof, wherein

the NADPH oxidase is a functional equivalent of the SEQ ID NO: 2 or has at least 50% sequence identity thereto. The claims are also drawn to said method comprising introducing into said plant or tissue, organ, part or cell thereof a NADPH oxidase antisense nucleic acid, a NADPH oxidase sense nucleic acid for co-suppression or a dsRNA NADPH oxidase. The claims are further drawn to said method wherein the plant pathogen is from a specific fungal species, and said plant is from a specific monocot plant species or a dicot plant. The claims are also drawn to a recombinant dsRNA capable of reducing expression of a NADPH oxidase, said recombinant dsRNA comprising a sense strand comprising a sequence which is essentially identical to at least part of the sense transcript of a sequence encoding the NADPH oxidase and antisense strand which essentially complementary to the sense strand, or comprising a functional equivalent of SEQ ID NO: 1; an expression cassette comprising at least part of a nucleic acid sequence encoding NADPH oxidase, operably linked to promoter in antisense and a vector comprising said expression cassette; and a transgenic organism comprising said vector.

Applicant teaches the isolated nucleic acid sequence of SEQ ID NO: 1, from barley, having a negative regulatory activity function upon attack by a powdery mildew of barley Blumeria graminis f.sp hordei (Bgh) and a method of reducing the NADPH oxidase expression in the epidermal cell by using NADPH oxidase dsRNA comprising SEQ ID NO: 1 (Examples 1-4).

Applicant has not taught methods of reducing NADPH oxidase activity/amount/function in a plant other than the method of transforming the plant or the

use of nucleic acids other than those encoding NADPH oxidase dsRNA having the ability to inhibit expression, amount and activity of an endogenous NADPH oxidase. The scope of claims 1-3 and 6-9 encompasses the use of any nucleic acid, not necessarily a NADPH oxidase nucleic acids, to inhibit the activity/amount/function of NADPH oxidase in a plant. Applicant has not provided guidance for the obtention and use of the NADPH oxidase sequences as broadly claimed or methods of their use in any organism. Applicant has not taught other methods of reducing activity/function/amount of NADPH oxidase in a plant and that resulted in increased resistance to plant pathogens. No guidance has been provided for a method other than transient transformation of barley cells with dsRNA comprising the unmodified sequence of SEQ ID NO: 1 and the evaluation of the development of powdery mildew in said barley genotype. Applicant has not provided guidance for any modifications to SEQ ID NO: 1 that resulted in DNA sequences encoding functional equivalents of SEQ ID NO: 2 or polypeptides having at least 50% identity thereto and retaining the desired function. Applicant has not provided guidance for the use of the exemplified and non-exemplified NADPH oxidase sequences in organisms other than plants and microorganisms. The specification is completely silent with respect to how to use NADPH oxidase sequences in animals to induce disease resistance.

The state of the prior art teaches unpredictability inherent in using antisense sequences to inhibit expression of endogenous protein to induce disease resistance in a plant. For example, Schiene et al (Mol Gen Genet (2000) 263:761-770) teach transformation of tobacco plants with an antisense construct from Alfalfa failed to

produce the expected disease resistant in tobacco plants (see Tables 1-3 and pages 765-767).

The state of the art for isolating genes with specified function is highly unpredictable. Substantial guidance is required with respect to hybridization/wash conditions that would allow the specific isolation of the target genes. In the absence of such guidance, one skilled in the art has to proceed with trial and error experimentation to screen through the vast number of cDNA and genomic clones to identify those genes capable of reducing amount/activity/function of a NADPH oxidase in a plant cell, and to evaluate the ability of said genes to increase plant disease resistance against iron deficiency in any organism.

Therefore, given the lack of guidance in the specification and in the prior art; the scope of the claims encompassing the use of NADPH sequences from any source to inhibit expression/level/amount of NADPH oxidase in any organism including animals; the unpredictability inherent in using antisense constructs to induce defense response in heterologous plant species as evidence by Schiene et al above, and the nature of the invention, as discussed above, the claimed invention cannot be practiced throughout the broad scope , therefore, the invention is not enabled. See, In re Wands 858 F.2d 731, 8USPQ2nd 1400 (Fed. Cir.1988). See also, *In re Fischer, 166 USPQ 19 24 (CCPA 1970)* where the court determined that the scope of the claims must bear a reasonable correlation with the scope of the enablement.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to methods that employ nucleic acids that are described by function only, i.e., capable of reducing an amount/activity/function of a NADPH oxidase in a plant. The composition and structure of nucleic acids capable of reducing an amount/activity/function of a NADPH oxidase in a plant cell are unknown. Transgenic plants, expression cassettes, and vectors comprising said nucleic acids are not described. Methods that employ nucleic acids encoding functional equivalents of barley NADPH oxidase are not described because the identity and structure of said nucleic acids are not described and are not known in the prior art. In contrast, Applicant describes nucleic acids encoding dsRNA NADPH oxidases from barley comprising SEQ ID NO: 1, transgenic plants, expression cassette/vector comprising said nucleic acids, and methods that employ said nucleic acids. Applicant has not described a representative number of nucleic acids capable of reducing amount/function/activity of a NADPH oxidase in any organism.

In *Eli Lilly and Co.* 43 USPQ2d 1398 (Fed. Cir. 1997), the court stated:

An adequate written description of a DNA "requires a precise definition, such as by structure, formula, chemical name, or physical properties", not a mere wish or plan

for obtaining the claimed chemical invention... Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it; what is required is a description of the DNA itself (43 USPQ2d at 1404).

The court held that held that human insulin-encoding cDNA is not described by prophetic example, which sets forth only a general method for obtaining the human cDNA:

The name cDNA is not itself a written description of that DNA; it conveys no distinguishing information concerning its identity...Describing a method of preparing a cDNA or even describing the protein that the cDNA encodes...does not necessarily describe the DNA itself. No sequence information indicating which nucleotides constitute human cDNA appears in the patent, as appears for rat cDNA....Accordingly, the specification does not provide a written description of human cDNA (43 USPQ2d at 1405).

The description of a single species of rat cDNA was held insufficient to describe the broad genera of vertebrate or mammalian insulin:

"In claims to genetic material...a generic statement such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA', without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It doesn't define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function...does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is (43 USPQ2d at 1406).

The court continued:

"Thus...a cDNA is not defined by the mere name 'cDNA', even if accompanied by the name of the protein that it encodes, but requires a kind of specificity usually achieved by means of the recitation of the sequence of nucleotides that make up the cDNA...A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus". (43 USPQ2d at 1406). See also where the court teaches that the disclosure of a process for obtaining cDNA from a particular organism and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from the organism which would encode the protein from that organism, despite the disclosure of a cDNA

encoding that protein from another organism.

The *University of Rochester v. G.D. Searle* & Co., Inc.(, U.S. District Court, Western District of New York, Decision and Order No. 00-CV-6161L,) decided 05 March 2003, at page 8, bottom paragraph, that method claims are properly subjected to a written description requirement if the starting material which requires that method is itself inadequately described. The court specifically stated, "(T)he claimed method depends upon finding a compound that selectively inhibits PGHS-2 activity. Without such a compound, it is impossible to practice the claimed method of treatment. It means little to "invent" a method if one does not have possession of a substance that is essential to practicing that method. Without that substance, the claimed invention is more theoretical than real;..... and there is no meaningful possession of the method."

Therefore, for all the reasons discussed above, the claimed invention does not meet the current written description requirements. See, also, the Written description Examination Guidelines published in Federal Registry/Vol. 66, No.4/Friday, January 5, 2001/Notices).

Remarks

No claim is allowed.

The claims are deemed free of the prior art of record.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Medina A. Ibrahim whose telephone number is

(571)272-0797. The examiner can normally be reached on M-TH 8:00 am to 5:30 PM, and every other Friday from 8:00 AM to 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on 571-272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MAI
8/31/2009

/Medina A Ibrahim/
Primary Examiner, Art Unit 1638